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<110> CHUGAI SEIYAKU KABUSHIKI KAISHA

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<151> 1999-07-02

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Al	a	Thi	· 1	le	Ser	Sei	Gl	y G	ly	Ser	Ту	r T	hr	Туі	r Ty	r i	Pro	Asp	Ser	Val
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Ly	S	Gly	' Aı	g	Phe	Thr	· Ile	e Se	er i	Arg	As	рA	sn	Ala	Ly	'S I	Asn	Thr	Leu	Tyr
6	5						70)						75						80
Le	u	Gln	Me	et :	Ser	Ser	Let	ı Ly	s S	Ser	Gl	ı A	sp	Thr	Al	a N	<i>l</i> le t	Phe	Tyr	Cys
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Ser	Va	al]	Lys	Le	eu T	hr (Cys	Thr	Le	eu S	er	Ser	. G	ln I	lis	Se	r T	hr T		hr
					20						25							30	· -	
He	G]	u I	Γrp	Hi	s G	ln (Gln	Gln	Pr	o G	lu	Lys	G	ly F	ro	Ar		yr L	eu M	et
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Lys	Le	u I	уs	Gl	n A	sp (Gly	Ser	Hi	s Se	er	Thr	G	ly A	sp	Gly	y I	le P	ro As	sp
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Asp Leu Lys Gln Asp Gly Ser His Ser Thr Gly Asp Gly Ile Pro Asp 50 55 60

Arg Phe Ser Gly Ser Ser Ser Gly Ala Glu Arg Tyr Leu Thr Ile Ser 65 70 75 80

Ser Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gly Val Gly Asp 85 90 95

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Ser	Leu	Gln	Ser		Asp	Glu	Ala	Asp		Tyr	Cys	Gly	Val	Gly	Asp
				85			_		90					95	
Thr	He	Lys		Gln	Phe	Val	Tyr		Phe	Gly	Gly	Gly		Lys	Leu
T)	37 1	T	100	01	T)			105					110		
Inr	Val		GIY	GIn	Pro										
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1	LCu	141	LCU	5	OIII	OC I	110	OC I	10	Ser	nia	SCI.	ԻԸՈ	15	ита
	Val	Lvs	Len		Cvs	Thr	Leu	Ser		Gln	His	Ser	Thr		Thr

Ile	Glu	Trp	Tyr	Gln	Gln	Gln	Pro	Glu	Lys	Gly	Pro	Arg	Tyr	Val	Met
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Gln Val Gl	ln Leu V	al Gl	u Ser	Gly (Gly G	ly Va	al Va	al Gi	n Pi	ro G	lv A	rg
1		5				10					15 15	• 0
Ser Leu Ar	g Leu S	er Cys	s Ala	Ala S	er G	ly Pl	ne Th	nr Ph	ie Se			vr
	20				25					10	- 4.	, -
Gly Met Se	r Trp V	al Arg	g Gln	Ala P	ro G	ly Ly	's Gl	у Le			p Va	ıl

35 40 45 Ala Thr Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Pro Asp Ser Val 50 55 60 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 65 70 75 80 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95 Ala Arg Gln Thr Thr Met Thr Tyr Phe Ala Tyr Trp Gly Gln Gly Thr 100 105 110 Leu Val Thr Val Ser Ser 115 <210> 57 <211> 411 <212> DNA <213> Mus musculus <220> <221> CDS <222> (1)... (411) <220> <221> mat_peptide <222> (58).. (411) <400> 57

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Met Asn Phe Gly Leu Ser Leu Ile Phe Leu Ala Leu Ile Leu Lys Gly

-10

-15

48

-5

gt	c ca	g tg	t gag	g gte	ca:	a cte	ggtg	g gag	g tci	t ggs	g gg	a gao	: tta	gt	g aa	g 96
Va	l Gl	n Cy	s Glı	ı Val	Glı	ı Let	ı Val	Glı	ı Sei	r Gly	y Gly	y Asr	Lei	ı Va	l Ly:	S
		-	1 1	l			5)				10)			
cci	gg	a gg	g tco	ctg	aaa	ctc	tcc	tgt:	gca	gco	tct:	gga	tto	ac	t tto	c 144
Pro	Gl	y Gl	y Sei	Leu	Lys	Leu	Ser	Cys	. Ala	Ala	Ser	Gly	Phe	Thi	r Phe	9
	18	5				20					25					
agt	ago	c tai	ggc	atg	tct	tgg	att	cgc	cag	act	cca	gac	aag	agg	g cte	s 192
Ser	Sei	Туі	Gly	Met	Ser	Trp	Ile	Arg	Gln	Thr	Pro	Asp	Lys	Arg	Leu	ľ
30	 				35					40					45	
gag	tgg	gto	gca	acc	att	agt	agt	ggt	ggt	agt	tac	acc	tac	tat	cca	240
Glu	Trp	Val	Ala	Thr	Ile	Ser	Ser	Gly	Gly	Ser	Tyr	Thr	Tyr	Tyr	Pro	
				50					55					60		
gac	agt	gtg	aag	ggg	cga	ttc	acc	atc	tcc	aga	gac	aat	gcc	aag	aac	288
Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	
			65					70					75			
acc	cta	tac	ctg	caa	atg	agc	agt	ctg	aag	tct	gag	gac	aca	gcc	atg	336
Thr	Leu	Tyr	Leu	Gln	Met	Ser	Ser	Leu	Lys	Ser	Glu	Asp	Thr	Ala	Met	
		80					85					90				
ttt	tac	tgt	gca	aga	cag	act	ac t	atg	act	tac	ttt	gct	tac	tgg	ggc	384
Phe	Tyr	Cys	Ala	Arg	Gln	Thr	Thr	Met	Thr	Tyr	Phe	Ala	Tyr	Trp	Gly	
	95					100					105					
caa	ggg	act	ctg	gtc	ac t	gtc	tct	gca								411
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser .	Ala								
110					115											
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75

336

70

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<211> 9

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                                85
                                                    90
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                                                                      384
  Tyr Tyr Cys Ala Arg Gln Thr Thr Met Thr Tyr Phe Ala Tyr Trp Gly
       95
                          100
                                               105
 cag gga acc ctg gtc acc gtc tcc tca
                                                                      411
 Gln Gly Thr Leu Val Thr Val Ser Ser
 110
                      115
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Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala
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                  5
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 Pro Tyr Trp Met Gln
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Ser Ile Phe Gly Asp Gly Asp Thr Arg Tyr Ser Gln Lys Phe Lys Gly
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Gly Leu Arg Arg Gly Gly Tyr Tyr Phe Asp Tyr

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10

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<222> (58).. (411)

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Met Ala Trp Thr Pro Leu Phe Phe Phe Phe Val Leu His Cys Ser Gly

-15

-10

-5

tet tte tee caa ett gtg ete aet eag tea tet tea gee tet tte tee 96

Ser Phe Ser Gln Leu Val Leu Thr Gln Ser Ser Ser Ala Ser Phe Ser

-1 1

5

10

ctg gga gcc tca gca aaa ctc acg tgc acc ttg agt agt cag cac agt 144

Leu Gly Ala Ser Ala Lys Leu Thr Cys Thr Leu Ser Ser Gln His Ser

15

20

25

acg tac acc att gaa tgg tat cag caa cag cca ctc aag cct cct aag

Thr Tyr Thr	lle Glu Trp Tv	r Gln Gln Gli	n Pro Leu Lys Pr	o Pro Ivo
30	35		40	45
tat gtg atg		a gat gga ago	c cac agc aca gg	
			His Ser Thr Gl	
	50	55		60
att cct gat			ggt gct gat cgo	
			Gly Ala Asp Are	
	65	70	75 75	
agc att tcc	aac atc cag cca		gca atg tac atc	
			Ala Met Tyr Ile	
80		85	90	oys dry
gtg ggt gat a	aca att aag gaa	caa ttt gtg	tat gtt ttc ggc	ggt ggg 384
			Tyr Val Phe Gly	
95	100		105	
acc aag gtc a	act gtc cta ggt	cag ccc		411
Thr Lys Val T	Thr Val Leu Gly	Gln Pro		
110	115			
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Thr Lys Leu Thr Val Leu Gly Gln Pro

<210> 67

<211> 411

<212> DNA

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<220>

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<220>

<221> mat_pept ide

<222> (58).. (411)

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-15 -10 -5

tct ttc tcc cag ctt gtg ctg act caa tcg ccc tct gcc tct gcc tcc 96 Ser Phe Ser Gln Leu Val Leu Thr Gln Ser Pro Ser Ala Ser Ala Ser

-1 1 5 10

ctg gga gcc tcg gtc aag ctc acc tgc acc ttg agt agt cag cac agt 144 Leu Gly Ala Ser Val Lys Leu Thr Cys Thr Leu Ser Ser Gln His Ser

15 20 25

acg tac acc att gaa tgg tat cag cag cag cca gag aag ggc cct aag 192
Thr Tyr Thr Ile Glu Trp Tyr Gln Gln Gln Pro Glu Lys Gly Pro Lys
30 35 40 45

tac ctg atg gat ctt aag caa gat gga agc cac agc aca ggt gat ggg 240

Tyr Leu Met Asp Leu Lys Gln Asp Gly Ser His Ser Thr Gly Asp Gly 50 55 60 att cct gat cgc ttc tca ggc tcc agc tct ggg gct gag cgc tac ctc 288 Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Ala Glu Arg Tyr Leu 65 70 75 acc atc tcc agc ctc cag tct gag gat gag gct gac tat tac tgt ggt 336 Thr lle Ser Ser Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gly 80 85 90 gtg ggt gat aca att aag gaa caa ttt gtg tac gtg ttc ggc gga ggg 384 Val Gly Asp Thr Ile Lys Glu Gln Phe Val Tyr Val Phe Gly Gly Gly 95 100 105 acc aaa ctg acc gtc cta ggc cag ccc 411 Thr Lys Leu Thr Val Leu Gly Gln Pro 110 115 <210> 68 <211> 411 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (1).. (411) <220> <221> mat_peptide <222> (58).. (411)

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				-	15					-1	0				_	-5		
tc	t tt	c to	c ca	ag c	t t	gtg	cte	ac	t ca	a tc	g cc	c tc	t gc	c tc	t go	c	tcc	96
Se	r Ph	e Se	er G	ln L	eu	Val	Leu	Th	r Gla	n Sei	r Pr	o Se	r Ala	a Se	r Al	a S	Ser	
		_	1	1				5	5				1()				
cts	g gg	a gc	c to	g g	tc	aag	ctc	acc	t go	c acc	e ttį	g ag	t agt	t cas	g ca	c a	agt	144
Leı	ı Gly	v Al	a Se	r Va	al	Lys	Leu	Thr	Cys	S Thi	Lei	ı Se	r Sei	Glr	ı Hi	s S	Ser	
	15	5					20					25	5					
ace	tac	ac	c at	t ga	aa	tgg	tat	cag	cae	cag	cca	a gag	g aag	ggc	cc	t a	ag	192
Thr	Tyr	Th	r II	e Gi	lu '	Trp	Tyr	Gln	Gln	Gln	Pro	Glu	Lys	Gly	Pro	o L	уs	
30)					35					40)					45	
tac	gtg	ate	g ga	t ct	t a	aag	caa	gat	gga	agc	cac	agc	aca	ggt	gat	g	gg	240
Tyr	Val	Met	As:	p Le	u I	Lys	Gln	Asp	Gly	Ser	His	Ser	Thr	Gly	Asr	G	ly	
				5	0					55					60	ì		
att	cct	gat	cg	e tt	c t	ca	ggc	tcc	agc	tct	ggg	gct	gag	cgc	tac	c	tc	288
Ile	Pro	Asp	Ar	g Ph	e S	Ser (Gly	Ser	Ser	Ser	Gly	Ala	Glu	Arg	Tyr	Le	eu	
			65	5					70					75				
													tat					336
Thr	He	Ser	Sei	Le	u G	dln S	Ser	Glu	Asp	Glu	Ala	Asp	Tyr	Tyr	Cys	GI	ly	
		80						85					90					
gtg	ggt	gat	aca	at	t a	ag g	gaa	caa	ttt	gtg	tac	gtg	ttc	ggc	gga	gg	g	384
Val	Gly	Asp	Thr	He	e L	ys (Glu (Gln	Phe	Val	Tyr	Val	Phe	Gly	Gly	Gl	У	
	95					1	.00					105						
acc	aaa	ctg	acc	gto	c	ta g	gc (cag	ссс									411
Thr	Lys	Leu	Thr	Val	Le	eu G	ly (Gln 1	Pro									
110					1.	15												

<210> 69

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<221> CDS
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-1 1 5 10

ctg gga gcc tcg gtc aag ctc acc tgc acc ttg agt agt cag cac agt 144
Leu Gly Ala Ser Val Lys Leu Thr Cys Thr Leu Ser Ser Gln His Ser

15 20 25

acg tac acc att gaa tgg tat cag cag cag cca gag aag ggc cct agg 192
Thr Tyr Thr Ile Glu Trp Tyr Gln Gln Gln Pro Glu Lys Gly Pro Arg
30 35 40 45

tac ctg atg gat ctt aag caa gat gga agc cac agc aca ggt gat ggg 240

Tyr Leu Met Asp Leu Lys Gln Asp Gly Ser His Ser Thr Gly Asp Gly

50 55 60

att cct gat cgc ttc tca ggc tcc agc tct ggg gct gag cgc tac ctc 288



Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Ala Glu Arg Tyr Leu 65 70 75 acc atc tcc agc ctc cag tct gag gat gag gct gac tat tac tgt ggt 336 Thr Ile Ser Ser Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gly 80 85 90 gtg ggt gat aca att aag gaa caa ttt gtg tac gtg ttc ggc gga ggg 384 Val Gly Asp Thr Ile Lys Glu Gln Phe Val Tyr Val Phe Gly Gly 95 100 105 acc aaa ctg acc gtc cta ggc cag ccc 411 Thr Lys Leu Thr Val Leu Gly Gln Pro 110 115 <210> 70 <211> 411 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (1).. (411) <220> <221> mat_peptide <222> (58).. (411) <400> 70 atg gcc tgg act cct ctc ttc ttc ttc ttt gtt ctt cat tgc tca ggt 48

-5

-10

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-15

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tet tte tee eag ett gtg etg aet eaa teg eee tet gee tee
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Ser Phe Ser Gln Leu Val Leu Thr Gln Ser Pro Ser Ala Ser Ala Ser
                              5
                                                  10
         -1
              1
ctg gga gcc tcg gtc aag ctc acc tgc acc ttg agt agt cag cac agt
                                                                   144
Leu Gly Ala Ser Val Lys Leu Thr Cys Thr Leu Ser Ser Gln His Ser
                         20
                                             25
     15
acg tac acc att gaa tgg tat cag cag cag cca gag aag ggc cct agg
                                                                   192
Thr Tyr Thr Ile Glu Trp Tyr Gln Gln Gln Pro Glu Lys Gly Pro Arg
 30
                     35
                                         40
                                                              45
                                                                   240
tac gtg atg gat ctt aag caa gat gga agc cac agc aca ggt gat ggg
Tyr Val Met Asp Leu Lys Gln Asp Gly Ser His Ser Thr Gly Asp Gly
                                     55
                                                          60
                 50
                                                                   288
att cct gat cgc ttc tca ggc tcc agc tct ggg gct gag cgc tac ctc
Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Ala Glu Arg Tyr Leu
             65
                                 70
                                                      75
acc atc tcc agc ctc cag tct gag gat gag gct gac tat tac tgt ggt
                                                                   336
Thr Ile Ser Ser Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gly
                             85
                                                 90
         80
gtg ggt gat aca att aag gaa caa ttt gtg tac gtg ttc ggc gga ggg
                                                                   384
Val Gly Asp Thr Ile Lys Glu Gln Phe Val Tyr Val Phe Gly Gly
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     95
                        100
                                                                   411
acc aaa ctg acc gtc cta ggc cag ccc
Thr Lys Leu Thr Val Leu Gly Gln Pro
110
                    115
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75

336

70

acc atc tcc agc ctc cag tct gag gat gag gct gac tat atc tgt ggt

65

Thr Ile Ser Ser Leu Gln Ser Glu Asp Glu Ala Asp Tyr Ile Cys Gly 80 85 90 gtg ggt gat aca att aag gaa caa ttt gtg tac gtg ttc ggc gga ggg 384 Val Gly Asp Thr Ile Lys Glu Gln Phe Val Tyr Val Phe Gly Gly 95 100 105 acc aaa ctg acc gtc cta ggc cag ccc 411 Thr Lys Leu Thr Val Leu Gly Gln Pro 110 115 <210> 72 <211> 411 <212> DNA <213> Homo sapiens <220> <221> CDS <222> (1).. (411) <220> <221> mat_peptide <222> (58).. (411) <400> 72 atg gcc tgg act cct ctc ttc ttc ttc ttt gtt ctt cat tgc tca ggt 48 Met Ala Trp Thr Pro Leu Phe Phe Phe Phe Val Leu His Cys Ser Gly -15-10-5 tet tte tee cag ett gtg etg act caa teg eec tet gee tet gee tee 96 Ser Phe Ser Gln Leu Val Leu Thr Gln Ser Pro Ser Ala Ser Ala Ser -1 1 5 10

_ 4		_	,													
															c agt	
Le	u Gl	y Ala	a Se	r Va	l Lys	Lei	ı Thi	r Cys	Thi	Leu	ı Ser	Sei	Gli	n His	s Ser	
	1	5				20)				25					
ac.	g tao	c acc	ati	gaa	a tgg	tat	cag	cag	cae	cca	gag	aag	ggo	c cci	agg	192
Th	r Tyı	r Thr	Ile	Glu	ı Trp	Туг	Gln	Gln	Gln	Pro	Glu	Lys	Gly	7 Pro	Arg	
30					35					40					45	
ta	c cte	gatg	gat	ctt	aag	caa	gat	gga	agc	cac	agc	aca	ggt	gat	ggg	240
															Gly	
				50					55					60		
att	cct	gat	cgc	ttc	tca	ggc	tcc	agc	tct	ggg	gct	gag	cgc	tac	ctc	288
He	Pro	Asp	Arg	Phe	Ser	Gly	Ser	Ser	Ser	Gly	Ala	Glu	Arg	Tyr	Leu	
			65					70					75			
acc	atc	tcc	agc	ctc	cag	tct	gag	gat	gag	gct	gac	tat	atc	tgt	ggt	336
Thr	Ile	Ser	Ser	Leu	Gln	Ser	Glu	Asp	Glu	Ala	Asp	Tyr	He	Cys	Gly	
		80					85					90				
gtg	ggt	gat	aca	att	aag	gaa	caa	ttt	gtg	tac	gtg	ttc	ggc	gga	ggg	384
		Asp														
	95					100					105					
acc	aaa	ctg	acc	gtc	cta	ggc	cag	ссс								411
Thr	Lys	Leu	Thr	Val	Leu (Gly	Gln :	Pro								
110					115											

<210> 73

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<212> DNA

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<222> (58).. (411)

<400> 73

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tet tte tee eag ett gtg etg act eaa teg eec tet gee tet gee tee 96 Ser Phe Ser Gln Leu Val Leu Thr Gln Ser Pro Ser Ala Ser Ala Ser -1 5 10

ctg gga gcc tcg gtc aag ctc acc tgc acc ttg agt agt cag cac agt 144 Leu Gly Ala Ser Val Lys Leu Thr Cys Thr Leu Ser Ser Gln His Ser 15 20 25

acg tac acc att gaa tgg tat cag cag cag cca gag aag ggc cct aag 192 Thr Tyr Thr Ile Glu Trp Tyr Gln Gln Gln Pro Glu Lys Gly Pro Lys 30 35 40 45

tac gtg atg gat ctt aag caa gat gga agc cac agc aca ggt gat ggg 240 Tyr Val Met Asp Leu Lys Gln Asp Gly Ser His Ser Thr Gly Asp Gly 50 55

att cct gat cgc ttc tca ggc tcc agc tct ggg gct gag cgc tac ctc 288 Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Ala Glu Arg Tyr Leu 65 70 75

acc atc tcc agc ctc cag tct gag gat gag gct gac tat atc tgt ggt 336 Thr Ile Ser Ser Leu Gln Ser Glu Asp Glu Ala Asp Tyr Ile Cys Gly 80 85 90

gtg ggt gat aca att aag gaa caa ttt gtg tac gtg ttc ggc gga ggg 384

60

Val Gly Asp Thr Ile Lys Glu Gln Phe Val Tyr Val Phe Gly Gly Gly 95 100 105

acc aaa ctg acc gtc cta ggc cag ccc

411

Thr Lys Leu Thr Val Leu Gly Gln Pro

110

115

<210> 74

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<220>

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-15

-10

-5

tct ttc tcc cag ctt gtg ctg act caa tcg ccc tct gcc tct gcc tcc 96 Ser Phe Ser Gln Leu Val Leu Thr Gln Ser Pro Ser Ala Ser Ala Ser

-1 1

5

10

ctg gga gcc tcg gtc aag ctc acc tgc acc ttg agt agt cag cac agt 144 Leu Gly Ala Ser Val Lys Leu Thr Cys Thr Leu Ser Ser Gln His Ser

15

20

25

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Thr	Tyr	Thr	Ile	Glu	Trp	Tyr	Gln	Gln	Gln	Pro	Glı	ı Lys	Gly	Pro	Arg	
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tac	gtg	atg	gat	ctt	aag	caa	gat	gga	agc	cac	ago	aca	ggt	gat	ggg	240
Tyr	Val	Met	Asp	Leu	Lys	Gln	Asp	Gly	Ser	His	Ser	Thr	Gly	Asp	Gly	
				50					55					60		
att	cct	gat	cgc	ttc	tca	ggc	tcc	agc	tct	ggg	gct	gag	cgc	tac	ctc	288
Ile	Pro	Asp	Arg	Phe	Ser	Gly	Ser	Ser	Ser	Gly	Ala	Glu	Arg	Tyr	Leu	
			65					70					75			
acc	atc	tcc	agc	ctc	cag	tct	gag	gat	gag	gct	gac	tat	atc	tgt	ggt	336
Thr	Ile	Ser	Ser	Leu	Gln	Ser	Glu	Asp	Glu	Ala	Asp	Tyr	Ile	Cys	Gly	
		80					85					90				
gtg	ggt	gat	aca	att	aag	gaa	caa	ttt	gtg	tac	gtg	ttc	ggc	gga	ggg	384
Val	Gly	Asp	Thr	He	Lys	Glu	Gln	Phe	Val	Tyr	Val	Phe	Gly	Gly	Gly	
	95					100					105					
acc	aaa	ctg	acc	gtc	cta	ggc	cag	ccc								411
Thr	Lys	Leu	Thr	Val	Leu	Gly	Gln	Pro								
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<213> Homo sapiens

Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly Lys Ser Ile Gln

1 5 10 15

Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile Ala Glu Ile His
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